

WHAT IS CLAIMED IS:

1. A method for selecting a clone of an ES cell containing a mutation in a gene that is expressed in a test cell comprising:

5 (a) providing cDNA obtained by reverse transcription of mRNA of the test cell;

(b) providing a collection of cultured ES cells organized into individual clones, wherein each clone is of an ES cell having a mutation in an exon in its genome, the mutation being in a different exon in cells of different clones;

10 (c) providing an array of different single stranded polynucleotides, the polynucleotides being fragments of exons containing mutations in (b);

(d) exposing the cDNA to the array under conditions permitting hybridization of polynucleotides in the array to nucleic acids;

15 (e) detecting hybridization of cDNA to a polynucleotide on the array; and,

(f) selecting a clone in the collection from which a hybridizing polynucleotide detected at (c) is an exon fragment.

2. The method of claim 1, wherein the ES cells are murine.

3. The method of claim 1, wherein mutations in the ES cells are as a result of introducing an exon trap vector into ES cells.

4. The method of claim 1, wherein the array is a nucleic acid microarray.

5. The method of claim 4, wherein the microarray comprises at least 500 different polynucleotides on a solid support surface.

6. The method of claim 5, wherein the microarray comprises at least about 1,000 different polynucleotides.

30 7. The method of claim 1, wherein the cDNA is labelled to facilitate detection at (e).

8. The method of claim 7, wherein the label is fluorescent or radioactive.

9. The method of claim 1, wherein selecting a clone comprises physically segregating a  
5 sample of ES cells from a selected clone.

10. A method for comparing gene expression between test cells, comprising:

(a) providing at least two cDNA samples, each sample obtained by reverse transcription of mRNA of a different test cell;

10 (b) providing a collection of cultured ES cells organized into individual clones, wherein each clone is of an ES cell having a mutation in an exon of its genome, the mutation being in a different exon in cells of different clones;

(c) providing at least one array of different single stranded polynucleotides, the polynucleotides being fragments of exons containing mutations in (b);

15 (d) exposing the cDNA samples to the at least one array under conditions permitting hybridization of polynucleotides on the array to nucleic acids;

(e) detecting hybridization of polynucleotides in the at least one array resulting from exposure to cDNA;

20 (f) selecting clones in the collection from which hybridizing polynucleotides detected at (e) are exon fragments; and,

(g) comparing a clone or clones which comprise exon fragments that hybridize to one of the cDNA samples to a clone or clones which comprise exon fragments that hybridize to another of the cDNA samples.

25 11. The method of claim 10, wherein the ES cells are murine.

12. The method of claim 10, wherein mutations in the ES cells are as a result of introducing an exon trap vector into ES cells.

30 13. The method of claim 10, wherein the array is a nucleic acid microarray.

14. The method of claim 13, wherein the microarray comprises at least 500 different polynucleotides on a solid support surface.

5 15. The method of claim 14, wherein the microarray comprises at least 1,000 different polynucleotides.

16. The method of claim 10, wherein the cDNA is labelled to facilitate detection at (e).

10 17. The method of claim 16, wherein the label is fluorescent or radioactive.

18. The method of claim 10, wherein selecting a clone comprises physically segregating a sample of ES cells from a selected clone.

15 19. A system for testing expression of a gene in a test cell, comprising:

(a) a collection of cultured ES cells organized into individual clones, wherein each clone is of an ES cell having a mutation in an exon of its genome, the mutation being in a different exon in cells of different clones; and,

20 (b) an array comprising at least 500 different single stranded polynucleotides on a solid support surface, the polynucleotides being fragments of the exons containing mutations in (a).

20. The system of claim 19, wherein the array comprises at least about 1,000 different polynucleotides.

25

21. The system of claim 19, wherein the array comprises at least about 10,000 different polynucleotides.

22. The system of claim 19, wherein the array is a nucleic acid microarray.

30

23. The system of claim 19, wherein the system additionally comprises a recorded index associating a position in the array at which a polynucleotide is present, to a clone comprising that polynucleotide in an exon in which there is a mutation.

5 24. The system of claim 23, wherein the recorded index is stored on a computer-readable medium.

25. The system of claim 19, wherein the ES cells are murine.

10 26. An exon trap vector comprising, in a 5' to 3' direction:

- (a) an unpaired splice acceptor;
- (b) a region encoding a reporter;
- (c) one or more polyadenylation signals;
- (d) a promoter functional in an ES cell;
- (e) a segment encoding a second reporter under transcriptional control of promoter (d); and,
- (f) an unpaired splice donor,

15 wherein the construct additionally comprises a selectable region of 300 base pairs or less between (a) and (b) or between (e) and (f).

20

27. The vector of claim 26, wherein the selectable region encodes a selectable marker.

28. The vector of claim 26, wherein the selectable region is *supF*.

25 29. The vector of claim 26, wherein the selectable region is a recombination site.

30. The vector of claim 29, wherein the recombination site is selected from the group consisting of: *att*, *lox*, and *frt*.